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TITLE PAGE: CONCISE COMMUNICATION

Prevalence and risk factors of prolonged QT interval and electrocardiographic abnormalities in persons living with HIV

Running head: “Prolonged QTc and electrocardiographic abnormalities in HIV infection”

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Abnormal electrocardiograms (ECG) are associated with increased risk of arrhythmias and sudden cardiac death. We aimed to investigate the prevalence and associated risk factors of prolonged QTc and major ECG abnormalities, in persons living with HIV (PLWH) and uninfected controls.

DESIGN

PLWH aged ≥ 40 were recruited from the Copenhagen comorbidity in HIV infection (COCOMO) study and matched on sex and age to uninfected controls from the Copenhagen General Population Study.

METHODS

ECGs were categorized according to Minnesota Code Manual of ECG Findings definition of major abnormalities. A QT interval corrected for heart rate (QTc) >440 ms in males and >460 ms in females was considered prolonged. Pathologic Q-waves were defined as presence of major Q-wave abnormalities.

RESULTS

ECGs were available for 745 PLWH and 2,977 controls. Prolonged QTc was prevalent in 9% of PLWH and 6% of controls, $p=.052$. Pathologic Q-waves were more common in PLWH (6%) than in controls (4%), $p=.028$. There was no difference in prevalence of major ECG abnormalities between PLWH and controls, $p=.987$.

In adjusted analyses, HIV was associated with a 3.6ms[1.8-5.4] longer QTc interval, $p<.001$, and HIV was independently associated with prolonged QTc (adjusted odds ratio: 1.59 [1.14-2.19]), $p=.005$. HIV was borderline associated to pathologic Q-waves after adjusting, $p=.051$.

CONCLUSION

HIV was associated with higher odds ratio of prolonged QTc after adjustment for cardiovascular risk factors, but analyses were not adjusted for QT-prolonging medication. Although evidence indicated more pathologic Q-waves in PLWH, the risk seemed to be associated mainly with an adverse risk profile.

Keywords HIV; ECG; EKG; QT interval; Abnormalities; Cardiovascular disease; Comorbidities

BACKGROUND

Previously, major electrocardiographic (ECG) abnormalities, including atrial fibrillation (AF), have been shown to be both prevalent and to carry a poor prognosis in persons living with HIV (PLWH)¹⁻³. Similarly, prolonged corrected QT interval (QTc) is common among PLWH and associated with malignant arrhythmias and sudden cardiac death (SCD)⁴, but few studies have compared the prevalence of prolonged QTc in PLWH and the uninfected population^{5,6}. Previous studies have included treatment naïve patients, patients from high risk populations, and patients with advanced HIV disease⁵⁻⁸. Thus, the effects of HIV on QTc may be confounded by an adverse risk profile with excess smoking, inflammation, and comorbidity (e.g structural heart disease) among PLWH⁹⁻¹³. Furthermore, use of QT-prolonging drugs may differ in PLWH¹⁴. Thus, to describe the effect of HIV infection on ECG abnormalities and prolonged QTc, a well-characterized population of PLWH and comparable uninfected controls is needed.

We aimed to determine the prevalence and associated risk factors of prolonged QTc and major electrocardiographic abnormalities among well-treated PLWH and uninfected controls and to determine if HIV is independently associated with prolonged QTc and/or major electrocardiographic abnormalities in PLWH. We hypothesized that HIV would be independently associated with prolonged QTc and major ECG abnormalities.

METHODS

Study populations and demographics

PLWH were recruited from the Copenhagen Co-morbidity in HIV Infection (COCOMO) Study (NCT02382822). The COCOMO study is a non-interventional cohort study which assess the burden and pathogenesis of non-AIDS comorbidities in PLWH. The procedures for recruitment and data collection have been described elsewhere⁹.

Uninfected controls were included from the Copenhagen General Population Study (CGPS), a non-interventional general population study¹⁵. All participants in COCOMO and a subset of CGPS participants older than 40 years of age had an electronic ECG recorded. COCOMO participants older than 40 were frequency matched by age and sex (1:4) to participants from CGPS.

Identical questionnaires were used to collect information regarding medical history, smoking, alcohol consumption and use of medication. A physical exam including anthropometrics and blood pressure was performed by trained clinical staff. Measurements of high-sensitivity C-reactive protein (hsCRP), LDL cholesterol (LDL) and glucose were done¹⁶. HIV-related characteristics were obtained through review of medical records.

We defined hypertension as current anti-hypertensive treatment and/or systolic ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg⁹. Body Mass Index (BMI) was defined according to the WHO classification¹⁷ and dyslipidemia was defined as LDL ≥ 160 mg/dl (4.14 mM) and/or current lipid lowering treatment⁹.

ECG recording

ECGs were recorded by trained using a CardioSoft electrocardiograph Module and CardioSoft v6.7 Diagnostic System (GE Healthcare) software.

A resting ECG was only recorded and stored when all lead readings were calibrated, and no muscular interference was visible. Recorded ECGs were transferred to the MUSE Cardiology Information System (GE Healthcare, Wauwatosa, WI) in standard 12SL output format.

ECG variables

ECGs were coded according to the Minnesota code manual for electrocardiographic findings (MC)¹⁸. AF, atrioventricular (AV) conduction abnormalities and length of intervals and

segments were coded using v.21 of the validated Marquette 12SL algorithm⁴. We prespecified to use Bazett's formula for QT interval correction. QT prolongation was defined as QTc >460ms for women and as QTc >450ms for men. Major prolongation was defined as QTc >480ms for both women and men¹⁹. Participants with a QRS duration of 120ms or more or with ventricular rates >100bpm, were not included in the analyses of the QT interval.

Electrocardiographic abnormalities were classified as major abnormalities as suggested by MC and according to similar studies^{6,20}(MC criteria in supplementary table 1 , <http://links.lww.com/QAD/B517>). All ECGs with major MC abnormalities were manually overread by a physician blinded to HIV status. Manually inspected ECGs of poor quality were excluded.

Statistics

Student's t tests or Mann–Whitney U tests were used for comparison of continuous data and χ^2 tests or Fisher's exact test were used for categorical data.

We assessed whether HIV was associated with prolonged QTc or major MC abnormalities using multivariable logistic regression analyses adjusted for a prespecified model. The model included age, sex, hypertension, diabetes, dyslipidemia and smoking status. We further tested if prespecified major MC abnormalities 1) pathologic Q-waves; 2) intraventricular blocks (IV-blocks); 3) AF were associated with HIV or other independent variables. We investigated the association of HIV and independent variables to QTc length in multiple linear regression adjusted for the same prespecified model. Within PLWH, we tested whether HIV-related characteristics including current cART use (protease inhibitors, Efavirenz and Rilpivirine) were associated with prolonged QTc or major MC abnormalities.

A *P*-value .05 inferred statistical significance. All analyses were generated as available case analysis using SAS software v9.4 (SAS Institute, USA.)

RESULTS

Of 3,735 coded ECGs, 484 met an MC criterion for major abnormality. On manual overreading of these, 13 (2%) were excluded due to inadequate quality and 32 (7%) were reclassified as *no abnormality*. ECGs were available for 745 PLWH and 2,977 controls (Supplementary Figure 1, <http://links.lww.com/QAD/B517>).

Patient characteristics are listed in Table 1.

Prolonged QTc among PLWH and uninfected controls

In PLWH and controls, mean QTc was 422ms (95% confidence interval[CI]: [421-424] and 421ms [420-421], respectively, $p=.049$ (Fig. 2). After adjusting, HIV was associated with 3.6ms [1.8-5.4] longer QTc interval, $p<.001$. Furthermore, age, female sex, hypertension, smoking, diabetes, obesity and hsCRP were associated with longer QTc (table 2).

Prolonged QTc was found in 9% of PLWH and in 6% of the controls, $p=.052$, corresponding to a crude odds ratio (OR) of 1.35 [1.00-1.83]. Major prolongation of the QTc was present in 1.3% of PLWH and 0.5% of controls, $p=.021$, but was not associated with HIV in adjusted analyses, $p=.168$ (Supplementary Figure 2, <http://links.lww.com/QAD/B517>).

After adjusting, HIV was independently associated with prolonged QTc with an adjusted odds ratio (aOR) of 1.59 [1.14-2.19], $p=.005$. Furthermore, older age, hypertension, and pathologic Q-waves were associated with prolonged QTc (table 2).

Prolonged QTc among PLWH

In analyses restricted to PLWH, current CD4, CD4 nadir <200 , CD8, CD4:CD8 ratio, previous AIDS defining condition, current use of protease inhibitor, Efavirenz or Rilpivirine, and illicit drug use were not independently associated with prolonged QTc.

Major abnormalities among PLWH and uninfected controls

A major MC abnormality was present in 88 (12%) of PLWH and in 351 (12%) of controls, $p=.987$. Pathologic Q-waves were found in 45 (6%) and 124 (4%) of PLWH and controls, respectively, corresponding to a crude odds ratio (OR) of 1.48 [1.04-2.10], $p=.028$. There was no difference in prevalence of IV-block $p=.839$, or AF $p=.285$, (Supplementary Table 2, <http://links.lww.com/QAD/B517>).

HIV was not independently associated with major MC abnormalities when adjusted for confounders, $p=.141$, or with any specific major MC abnormality, including AF ($p=.254$) or IV-blocks ($p=.723$). However, a borderline association with pathologic Q-waves was found ($p=.051$). In PLWH, but not controls, pathologic Q-waves were also associated with hsCRP (aOR per 10 mg/L increase: 1.36 [1.02-1.83]).

Discussion

PWLH had a higher prevalence of prolonged QTc compared to uninfected controls, and HIV was independently associated with prolonged QTc after adjusting for traditional risk factors, though we did not adjust for use of QT prolonging medications. cART regimen was not associated with prolonged QTc. Prevalence of pathologic Q-waves was higher among PLWH, but the association was attenuated when adjusting for traditional risk factors, suggesting that traditional risks may carry some of the excess risk.

Prolonged QTc is independently associated with malignant ventricular arrhythmias and SCD⁴, and has been reported to be higher among PLWH in both treatment naïve⁸ and patients on cART^{14,21}. Prevalence estimates differ markedly and ranges from 5% to more than 40%, depending on the investigated population. Most prior studies are limited by size, have lacked comparable controls or have recruited patients from highly selected populations^{8,14,21–23}. In the HIV-HEART study, prolonged QTc was present in 21% among PLWH vs 3.5% among

the uninfected¹⁴. In the MACS cohort, there was no difference in prevalence of prolonged QTc between PLWH and controls (3% in both groups), but the QTc interval was 4ms longer among PLWH when adjusting for confounders²¹. The association was attenuated by adjustment for inflammatory markers. The prevalence of prolonged QTc in our study was 9% and in between the estimates from the HIV-HEART and MACS cohorts and our data confirm the association between inflammation and QTc in other studies^{11,21}. hsCRP is, however, a crude marker of inflammation and further studies should explore the impact of different inflammatory pathways in PLWH and uninfected.

We expected major MC abnormalities to be prevalent among PLWH and while more than one in ten PLWH did have major MC abnormalities, prevalence was not higher than among the controls, as anticipated by prior studies without controls^{2,6}. HIV and pathologic Q-waves were associated in univariable analyses, but this association was attenuated to borderline significance after adjusting for traditional risk factors, suggesting an adverse risk profile among PLWH^{9,24} to contribute. PLWH have increased risk of heart failure and cardiomyopathies¹², and studies of intraventricular conduction defects in PLWH have found QRS-duration to be associated with use of protease inhibitors²⁵. We therefore hypothesized HIV infection to be associated with IV-block, but distribution of IV-blocks was similar in PLWH and controls and there was no association to specific cART regimens. A recent analysis of five thousand PLWH did not report AF to be more prevalent than in controls, but found low CD4 nadir to be predictive of AF³. In an indirect comparison to the Framingham study, a study found higher incidence of AF in PLWH aged 55-75, but they did not account for differences in risk factors². We found a low (1%) prevalence of AF in PLWH and controls and comparable to participants in Framingham²⁶. The few cases did not allow us to investigate associations between AF and CD4 nadir.

Common causes of acquired QTc prolongation include use of methadone and antiarrhythmic, antibiotic, and psychotropic medications which may all be more commonly used among PLWH^{27,28}. Limitations to the study, thus, included inability to adjust for QT prolonging medication use, and although MC criteria are validated against clinical outcomes, other categorizations may have produced different estimates of abnormalities. However, ECGs were recorded on the same device and grouped according to the same criteria, interval and segment lengths were automatically measured and all ECG evaluations were blinded to HIV status. Thus, a different categorization would likely have affected both populations equally. Additionally, the cross-sectional design prevents us from drawing conclusions regarding causality. Strengths of the study include the size and the uniform approach to data collection.

In conclusion, well-treated PLWH had a higher prevalence of prolonged QTc and pathologic Q-waves and ECG evidence of previous myocardial infarction than uninfected controls. Adjusting for risk factors attenuated the association between HIV and pathologic Q-waves, but HIV was *independently* associated with prolonged QTc. hsCRP was marginally associated with QTc length and pathologic Q-waves (but not prolonged QTc) in PLWH. Further studies are needed to explore the impact of prolonged QTc on clinical outcomes in PLWH.

References

1. Soliman E, Prineas R. Prevalence and Prognostic Significance of ECG Abnormalities in HIV-infected Patients: Results from the Strategies for Management of Antiretroviral Therapy (SMART) Study. *J* 2011;44(6):779-785.
doi:10.1016/j.jelectrocard.2010.10.027.Prevalence
2. Hsu JC, Li Y, Marcus GM, et al. Atrial fibrillation and atrial flutter in human immunodeficiency virus-infected persons: Incidence, risk factors, and association with markers of HIV disease severity. *J Am Coll Cardiol.* 2013;61(22):2288-2295.
doi:10.1016/j.jacc.2013.03.022
3. Sanders JM, Steverson AB, Pawlowski AE, et al. Atrial arrhythmia prevalence and characteristics for human immunodeficiency virus-infected persons and matched uninfected controls. *PLoS One.* 2018;13(3):e0194754. doi:10.1371/journal.pone.0194754
4. Nielsen JB, Graff C, Rasmussen P V., et al. Risk prediction of cardiovascular death based on the QTc interval: Evaluating age and gender differences in a large primary care population. *Eur Heart J.* 2014;35(20):1335-1344. doi:10.1093/eurheartj/ehu081
5. Charbit B, Rosier A, Bollens D, et al. Relationship between HIV protease inhibitors and QTc interval duration in HIV-infected patients: A cross-sectional study. *Br J Clin Pharmacol.* 2009;67(1):76-82. doi:10.1111/j.1365-2125.2008.03332.x
6. Soliman EZ, Prineas RJ, Roediger MP, et al. Prevalence and prognostic significance of ECG abnormalities in HIV-infected patients: Results from the Strategies for Management of Antiretroviral Therapy study. *J Electrocardiol.* 2011;44(6):779-785.
doi:10.1016/j.jelectrocard.2010.10.027
7. Gili S, Mancone M, Ballocca F, et al. Prevalence and predictors of long corrected QT interval in HIV-positive patients: A multicenter study. *J Cardiovasc Med.* 2017;18(7):539-

544. doi:10.2459/JCM.0000000000000436

8. Ogunmola O, Oladosu Y, Olamoyegun M. QT_c interval prolongation in HIV-negative versus HIV-positive subjects with or without antiretroviral drugs. *Ann Afr Med*. 2015. doi:10.4103/1596-3519.152072
9. Gelpi M, Afzal S, Lundgren J, et al. Higher Risk of Abdominal Obesity, Elevated LDL Cholesterol and Hypertriglyceridemia, but not of Hypertension, in People Living with HIV: Results from the Copenhagen Comorbidity in HIV Infection (COCOMO) Study. *Clin Infect Dis*. 2018;(May):1-8. doi:10.1093/cid/ciy146
10. Wu KC, Zhang L, Haberlen SA, et al. Predictors of electrocardiographic QT interval prolongation in men with HIV. *Heart*. 2018:heartjnl-2018-313667. doi:10.1136/heartjnl-2018-313667
11. Lazzerini PE, Capecechi PL, Laghi-Pasini F. Systemic inflammation and arrhythmic risk: Lessons from rheumatoid arthritis. *Eur Heart J*. 2017;38(22):1717-1727. doi:10.1093/eurheartj/ehw208
12. Feinstein MJ, Hsue PY, Benjamin LA, et al. Characteristics, Prevention, and Management of Cardiovascular Disease in People Living With HIV: A Scientific Statement From the American Heart Association. *Circulation*. 2019:1-27. doi:10.1161/CIR.0000000000000695
13. Nordell AD, McKenna M, Borges AH, et al. Severity of Cardiovascular Disease Outcomes Among Patients With HIV Is Related to Markers of Inflammation and Coagulation. *J Am Heart Assoc*. 2014;3(3):e000844-e000844. doi:10.1161/JAHA.114.000844
14. Reinsch N, Arendt M, Geisel MH, et al. Prolongation of the QT_c interval in HIV-infected individuals compared to the general population. *Infection*. 2017;45(5):659-667. doi:10.1007/s15010-017-1053-9

15. Nordestgaard BG, Benn M, Schnohr P, Tybjaerg-Hansen A. Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. *JAMA*. 2007;298(3):299-308. doi:10.1001/jama.298.3.299
16. Ronit A, Haissman J, Kirkegaard-Klitbo DM, et al. Copenhagen comorbidity in HIV infection (COCOMO) study: a study protocol for a longitudinal, non-interventional assessment of non-AIDS comorbidity in HIV infection in Denmark. *BMC Infect Dis*. 2016;16(1):713. doi:10.1186/s12879-016-2026-9
17. Consultation WHOE. Waist Circumference and Waist-Hip Ratio Report of a WHO Expert Consultation. *World Health*. 2008. doi:10.1038/ejcn.2009.139
18. Prineas RJ, Crow RS, Zhu-Ming Zhang. *The Minnesota Code Manual of Electrocardiographic Findings*. Vol 136. 2nd ed. Springer Berlin Heidelberg; 2010.
19. Rautaharju PM, Surawicz B, Gettes LS. AHA/ACCF/HRS Recommendations for the Standardization and Interpretation of the Electrocardiogram. Part IV: The ST Segment, T and U Waves, and the QT Interval A Scientific Statement From the American Heart Association Electrocardiography and Arrhythmias Co. *J Am Coll Cardiol*. 2009;53(11):982-991. doi:10.1016/j.jacc.2008.12.014
20. Auer R, Bauer DC, Marques-Vidal P, et al. Association of major and minor ECG abnormalities with coronary heart disease events. *JAMA - J Am Med Assoc*. 2012. doi:10.1001/jama.2012.434
21. Wu KC, Zhang L, Haberlen SA, et al. Predictors of electrocardiographic QT interval prolongation in men with HIV. *Heart*. 2018:heartjnl-2018-313667. doi:10.1136/heartjnl-2018-313667
22. Vallecillo G, Mojal S, Roquer A, et al. Risk of QTc prolongation in a cohort of opioid-dependent HIV-infected patients on methadone maintenance therapy. *Clin Infect Dis*.

2013. doi:10.1093/cid/cit467

23. Qaqa AY, Shaaban H, Debari VA, et al. Viral load and CD4+ cell count as risk factors for prolonged QT interval in HIV-infected subjects: A cohort-nested case-control study in an outpatient population. *Cardiology*. 2010;117(2):105-111. doi:10.1159/000320216
24. Helleberg M, Afzal S, Kronborg G, et al. Mortality attributable to smoking among HIV-1-infected individuals: A nationwide, population-based cohort study. *Clin Infect Dis*. 2013;56(5):727-734. doi:10.1093/cid/cis933
25. McIntosh RC, Lobo JD, Hurwitz BE. Current assessment of heart rate variability and QTc interval length in HIV/AIDS. *Curr Opin HIV AIDS*. 2017;12(6):528-533. doi:10.1097/COH.0000000000000408
26. Schnabel RB, Yin X, Gona P, et al. 50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham Heart Study: A cohort study. *Lancet*. 2015. doi:10.1016/S0140-6736(14)61774-8
27. Arizona Center for Education and Research on Therapeutics. COMBINED LIST OF DRUGS THAT PROLONG QT AND/OR CAUSE TORSADES DE POINTES (TDP). <https://crediblemeds.org/>. Accessed June 6, 2019.
28. Roden DM. Drug-induced prolongation of the QT interval. *N Engl J Med*. 2004. doi:10.1056/NEJMr032426

Table 1. Demographic characteristics of persons living with HIV and uninfected controls

Demographic characteristics		
	PLWH 745	Controls 2,977
Men, n (%)	641 (86)	2,481 (83)
Age, mean (SD)	54 (9)	56(9)
Origin		
• Scandinavian	571 (77)	2,782 (93)
• Other European	78 (11)	130 (4)
• Middle East and Indian subcontinent	12 (2)	19 (1)
• Other	82 (11)	9 (0.3)
Smoking status, n (%)		
• Current	195 (26)	365 (12)
• Former	292 (39)	1,284 (43)
• Never	257 (35)	1,303 (44)
Pack years median (IQR)	20 (7-34)	13 (3-26)
Hypertension, n (%)	348 (47)	1,861 (63)
Diabetes, n (%)	37 (5)	123 (4)
Obese (BMI>30)	73 (10)	538 (18)
LDL	2.8 (1)	3.2 (1)
Statin	120 (16)	388 (13)
Dyslipidemia	71 (10)	473 (16)
HIV specific characteristics		
Mode of transmission		
• MSM	520 (70)	-
• Heterosexual	161 (22)	-
• IDU	8 (1.1)	-
• Other or unknown	56 (7.5)	-
Current CD4 count, CD4/μL, median (IQR)	510 (670-870)	-
• <200 CD4/ μ L, n (%)	11 (1.5)	-
• 200–349 CD4/ μ L, n (%)	45 (6.0)	-
• 350-499 CD4/ μ L, n (%)	109 (15)	-
• >500 CD4/ μ L, n (%)	572 (77)	-
CD4 nadir <200/μL, n (%)	327 (44)	-
HIV RNA <50 copies/mL, n (%)	706 (95)	-
Current cART use, n (%)	732 (98)	-
• Rilpivirine use, n (%)	16 (2.3)	-
• Efavirenz use, n (%)	217 (30)	-
• Protease inhibitor use, n (%)	222 (30)	-
IDU: Injecting drug use; MSM:Men who have sex with men; Number of missing data per variable: Origin: 39; Smoking status:26; Hypertension:48; Diabetes:23; Obese:7; Dyslipidemia:127		

Table 2. Association of corrected QT interval to independent risk factors.

Association of corrected QT interval to independent risk factors *								
QTc length					Prolonged QTc			
	β -coefficient	P	Adjusted β -coefficient	P	OR	P	aOR	P
HIV yes vs. no	1.9 [0.0-3.7]	.049	3.6 [1.8-5.4]	<.001	1.35 [1.00-1.83]	.052	1.59 [1.14-2.19]	.005
Age*	3.0 [2.3-3.7]	<.001	2.9[2.1-3.7]	<.001	1.54 [1.34-1.77]	<.001	1.45 [1.25-1.67]	<.001
Male sex	-8.3 [-10.2-(-)6.5]	<.001	-11.2 [-13.1-(-)9.2]	<.001	1.03 [0.72-1.46]	.888	0.72 [0.51-1.06]	.086
Hypertension	6.0 [4.6-7.4]	<.001	5.8 [4.3-7.3]	<.001	2.34 [1.72-3.18]	<.001	1.94 [1.41-2.71]	<.001
Current smoker	1.6 [-0.4-3.5]	.114	2.6 [0.6-4.5]	.010	1.14 [0.81-1.62]	.453	1.26 [0.87-1.79]	.212
Dyslipidemia	1.1 [-0.9-3.1]	.297	1.4 [-0.5-3.4]	.149	1.12 [0.78-1.60]	.541	1.18 [0.81-1.68]	.368
Diabetes	1.4 [0.74-2.76]	.289	4.4 [0.9-8.0]	.014	2.01 [1.20-3.35]	.007	1.60 [0.91-2.66]	.086
hsCRP**	2.3 [0.8-3.9]	.002	1.5 [0.02-3.0]	.046	1.14 [0.90-1.36]	.196	1.07 [0.82-1.29]	.507
Heavy Drinker[‡]	1.6 [0.1-3.2]	.040	1.0 [-0.6-2.6]	.227	1.17 [0.89-1.55]	.263	0.94 [0.70-1.27]	.702
Obesity^{‡‡}	4.6 [2.7-6.5]	<.001	3.0 [1.1-5.0]	.002	1.43 [1.04-1.98]	.027	1.21 [0.85-1.68]	.287
Pathologic Q-waves	6.9 [3.3-10.5]	.001	5.6 [2.0-9.3]	.002	2.66 [1.66-4.28]	<.001	2.24 [1.33-3.64]	.002
Scandinavian (yes vs. no)	5.3 [2.6-8.0]	<.001	3.4 [0.7-6.0]	.014	1.49 [0.90-2.47]	.122	1.30 [0.80-2.25]	.317
<p>* Multiple linear regression analyses (left panel) and multivariable logistic analyses (right panel) with 95% confidence intervals. Model Adjusted for Age, Sex, Hypertension, Smoking status, Dyslipidemia and Diabetes.</p> <p>* per decade older</p> <p>** per 10 mg/L increase</p> <p>‡ defined as 14 or more units of alcohol per week</p> <p>‡‡ defined as BMI >30kg/m²</p> <p>OR: odds ratio; aOR: adjusted odds ratio; QTc: QT interval corrected for heart rate using Bazett's formula (QT/RR^{1/2}); prolonged QTc defined as QTc >460ms for women and as QTc >450ms for men</p>								